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Cutaneous and Systemic.

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THE TOXIC EFFECTS OF IODOFORM, CUTANEOUS AND SYSTEMIC.*

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AMONG the important advances which have been made within the past ten years in medicine and surgery, and particularly ætiology and therapeutics, the contributions to our knowledge of the toxic action of drugs, systemic and cutaneous, may, I think, deservedly take high rank. While, ten years ago, our knowledge of the toxic effects of drugs upon the skin was limited and fragmentary, to-day it is much more extended and far more systematic. Many drugs which were formerly thought to be harmless are now known to possess toxic properties which develop upon the skin. Indeed, in no department of medicine has more good work been done than in the study of drug eruptions, much of it, by the way, by American observers. It is pleasing to note that two monographs on this subject, showing wide and painstaking observation and much erudition, have appeared within the present year from the pens of two members of this association, Dr. White and Dr. Morrow. It is in the line of this good work that I venture to present this paper

* Read before the American Dermatological Association at its eleventh annual meeting.



upon the action of iodoform, which within the past seven years has been shown to possess the most subtle and formidable toxic qualities, systemic and cutaneous. Though a number of cases of the iodoform exanthem have been published, our knowledge of the subject is to-day incomplete and unsatisfactory. The literature is as follows: Zeissl reported two cases, 1881; Fifield one case, 1882; Fabre published two, Janowsky six, and from Neisser appeared a short article based on seven cases, in 1884; Goodell one case in 1885; Treves two cases and Köster-Syke one case in 1886; Koenig, in 1882, and Hoepfl, in 1883, spoke casually of erythema occurring in cases of iodoform poisoning. There are really, however, but sixteen cases on record from which definite information may be obtained. To these I add nine, seven of which occurred in my surgical and genito-urinary practice, and two were under the care of friends.

The histories of these cases, which I will give with all possible brevity, very clearly portray the multiform dermal changes due to this drug. Since the toxic action is largely and sometimes wholly systemic, the constitutional effects of the agent must also be considered in this essay.

Finally, the practical lessons drawn from my own experience and from my study of that of others, which are of interest to physicians and surgeons as well as dermatologists, will also be considered.

CASE I.—A man, aged twenty-one, in the fall of 1885 presented two small chancroids on the inner layer of the prepuce. He applied iodoform to the surface, and within three hours the whole penis and scrotum were red, swollen, and the seat of intense pruritus and burning. By the use of cooling lotions in the recumbent position, the inflammatory symptoms disappeared in three days. As the chancroids were still active, I touched them with an ethereal solution of iodoform (3j to ℥j), and in a few

hours an erythematous oedema, nearly as severe as the first, was produced. There was no systemic reaction.

CASE II.—A man, aged thirty-two, syphilitic four years, having extensive rupial syphilide, was under my care at Charity Hospital in the summer of 1884. So wretched was his condition that it was thought best to conciliate the stomach with easily digestible food before beginning internal medication. The crusts were soaked with oil, and those on the left leg removed at the first séance. The exposed ulcers were washed, and then quite freely dusted with iodoform, and the limb bandaged. That night the man slept very little, and complained of great burning and tension in the diseased parts. The next day a deep-red erythematous eruption had spread from the leg to the thigh. There was elevation of temperature, severe frontal headache, and giddiness and absolute anorexia. The erythema, which was very superficial, appeared about the neck and shoulders and increased rapidly, and merged with the invading erythema of the thigh, and in forty-eight hours covered the whole body. The appearances were those of scarlatina. There were no throat symptoms, nor had the patient taken quinine or any medicine surreptitiously. The use of iodoform was discontinued, and the rash faded, with decided exfoliation, in about four days.

CASE III.—A woman, aged twenty-eight, syphilitic four years, was admitted to Charity Hospital in the fall of the year 1882 for an extensive gummatous ulcer of the left leg. It was freely dusted with iodoform, and a retentive bandage applied. Two days later she complained of a burning and throbbing pain of the part. She had diarrhoea and vomiting, complained of great frontal pain, had delusions, and was utterly prostrated. An oedematous erythema, almost as pronounced as that of erysipelas, beginning in the bandaged leg, invaded the thighs, buttocks, and hypogastrium. Fully two weeks elapsed before this woman's local and general condition was as favorable as it was prior to the use of the iodoform. She had taken iodide of potassium prior to the appearance of this drug eruption, and did so afterward with impunity.

CASE IV.—A woman, aged twenty-six, in the fourth year of

syphilis, was attacked in June, 1885, with infiltration in the inguinal ganglia of the right side, which were excised and curetted. The case was much retarded by the constant appearance of new infiltrated ganglia. The woman's general condition was poor, and the wound cavity was slow to heal under iodoform and gauze. On the twelfth day, shortly after a healthy healing surface had been observed, the wound became unhealthy in appearance, its surface pale, flabby, secreting no pus, but a scanty and bloody serum. The integument around it upon the hypogastrium and groin became painful, red, and œdematous. Within twenty-four hours a patch, fully ten inches in diameter, was the seat of this erythema, which was sharply margined. On the second day groups of papules and papulo-vesicles and pustules developed, and the appearances were much like those of erythema multiformis of severe type. Under appropriate treatment the erythema fully disappeared by the eighth day. Coincidentally with the appearance of the rash the patient became weak, restless, dizzy, and drowsy. Temperature was 101° F., and urine was scanty and albuminous, but showed no casts nor blood. At no time was more than a drachm of iodoform used in the wound cavity, and just before the morbid outburst about half that quantity was used.

CASE V.—For the history of the following case I am indebted to my friend, Dr. A. G. Gerster. A. B., a laborer, aged thirty-four, was admitted into the German Hospital, January 2, 1887, on account of an ulcerated stump of the right thigh. Re-amputation was performed, January 7th, just above the condyles. Drainage-tubes were inserted, and the wound was dressed with iodoform and corrosive-sublimate gauze. On January 8th an intense erythema of thigh and thorax, also of face, arms and hands, and left lower extremity—in fact, of the whole body—appeared. Eruption resembled scarlet fever. The patient had not taken quinine. Severe itching was experienced all over body. No systemic symptoms were observed.

January 10th.—A change of dressing to boro-salicylic lotion was made. Wound united by primary adhesion. Erythema about the line of union, where the iodoform gauze had been applied, has become the seat of bullæ.

11th.—Erythema has disappeared, leaving desquamation over the thighs, abdomen, and gluteal regions.

CASE VI.—Zeissl's first case * was that of a boy three years of age upon whose leg was an ulcer which was dressed for fourteen days with iodoform, when his temperature rose to 105° F., and he became drowsy and vomited and passed albuminous urine. At this time a sharply outlined erythematous eruption appeared on the flexor aspect of the upper part of each arm and on the inner aspect of each thigh, with islands of unaffected skin. Discontinuance of the use of iodoform was followed by fading of the rash and cessation of the morbid symptoms. A second application caused a similar result in two days. After that the drug was still used and the patient became gradually accustomed to it, so that it no longer produced an inflammatory reaction.

CASE VII.—The second case was that of a man, aged thirty-six, having caries of the rib with sinus. This was treated with a pencil of iodoform every second day, when after ten days an erythema urticata in circumscribed patches appeared on the flexor aspects of the limbs.

CASE VIII.—Janowsky † reported the following five cases at the International Medical Congress at Copenhagen:

1. A man, aged twenty-eight, having soft chancres which were dusted with iodoform, was attacked with fever, and an erythema appeared on thighs, right hypogastrium, and lumbar region. The temperature remained elevated two days; the erythema extended to the left side and grew pale in three days. The iodoform being still used, the eruption invaded the forearms and disappeared in two days with desquamation. Temperature was normal during the latter part of the attack. In this case, as in others observed by this author, continued use of the drug caused a repetition of the appearance of the exanthem.

2. A man, aged twenty-two, had an ulcer on the sulcus glandis, and an open bubo, which was treated with a permanent iodoform dressing. In twenty-four hours an eruption of small

* "Zwei Fälle von Jod-Exanthem nach äusserlicher Anwendung des Iodoforms," "Allg. Wien. med. Ztg.," xxvi, 455, 1881.

† "Vierteljahrsschrift für Dermatologie und Syphilis," pp. 495 *et seq.*, 1884.

red papules appeared on the hypogastrium which in places became confluent. On the third day a similar eruption appeared on the left forearm, which later on, like the former, became a diffuse erythema. Still later the buttocks were similarly invaded. The eruptions disappeared rapidly, there being slight scaling. There was no fever at any time.

3. A man, aged thirty-one, had a scattered ulcerating syphilitide. Some of the ulcers on the legs were scraped and dressed with iodoform. On the next day the patient complained of severe itching on the thighs, and in two days a symmetrical eruption resembling erythema iris appeared on the thighs and legs which disappeared in two days with slight desquamation. Fourteen days later a similar application was made, and was followed by an erythema similar to the first one.

4. A man, aged twenty-four, had soft chancres on the penis, and a bubo, which had been incised and dressed with iodoform. Three days later there was a rise in temperature, and an erythema appeared on the surrounding parts and extended to the hip, the buttocks, and the chest. The congestion was so great that hæmorrhage took place from some of the papules seated on the erythematous surface. Three days after the substitution of bichloride gauze for the iodoform the eruption disappeared. But when the latter was again used, some days later, the eruption reappeared.

5. A man, aged forty-eight, had an ulcerated gumma of the left calf which was dressed with iodoform. No internal treatment was ordered. In three days an erythema appeared on the left thoracic region, the back, and the left shoulder-blade, accompanied with a mild but ephemeral fever. Very soon large bullæ formed on the reddened surface and ran a similar course to those of pemphigus.

CASE IX.—Dr. Köster-Syke * gives his personal experience very graphically as to the action of both carbolic acid and iodoform on the integument. The latter was to him a veritable poison, even if he merely came near it. A short time after using it

* "Hochgradige Idiosynkrasie gegen Iodoform und Karbol,"
"Deutsche Medizinal-Zeitung," April 26, 1886.

in his professional capacity he experienced a fearful itching of the whole body, slight elevation of temperature, and during the night his face and hands up to the elbows became red, swollen, and the seat of large bullæ. For three or four days so great was the swelling of the face that his eyes were closed. For a long time he ceased to use iodoform in his practice, but later on ventured to use it about the eyes of his patients, taking all precautions, even to wearing kid gloves, in order that none of the drug should come in contact with his skin. In spite of this care, in ten minutes he experienced itching on the hands and face, which during the evening became red and swollen. Such was his suffering from simply smelling the drug.

Not long ago I was consulted by a young man for obstinate ulceration of the prepuce following herpes, who requested me particularly not to prescribe iodoform, since upon two occasions when he had used it his room-mate had suffered severely from coryza and swelling of the eyelids.

CASE X.—Treves reports the following case: * A well-developed, healthy girl, aged thirteen, was admitted, in April, 1886, into the London Hospital with a simple ununited fracture of the left ulna. On May 8th the fracture was cut down upon and at first dressed with Lister's gauze, which, two days later, was replaced by iodoform. No ill effect of the drug was experienced until the end of May, when the wound had become very shallow. Then, when comparatively little iodoform was being used, on June 1st, the entire forearm became evenly swollen and œdematous, slightly red and tender. From this time on for several days there was elevation of temperature. Soon a crop of vesicles appeared on the morbid surface, limited to the forearm but not to the wound. On June 2d the use of iodoform was discontinued and the rash was healing. Three days later, after the discontinuance of the use of iodoform, after a few hours of severe headache and giddiness, a rash, limited to the left forearm, arm, and shoulder, made its appearance. In a day it spread to the neck, face, and chest. The eruption, seated on the erythematous surface, consisted of pin-head sized, pale-red

* "The Iodoform Rash," "Practitioner," October, 1886.

papules grouped together in clearly defined patches of the sizes of a five-cent nickel-piece and of a half-dollar. At the end of the second day the eruption had disappeared. On the day after its appearance the wound had assumed an unhealthy look. In a few days healing began and the patient was discharged cured.

CASE XI.—A man, aged twenty-seven, had, in January of this year, a suppurating bubo, which after incision I curetted, dusted the cavity with about a drachm of iodoform, and then stuffed it with plain gauze, retained by a spica bandage. During the night he suffered from great heat and itching in the wound, and on the following day at 5 P. M. I found an erythematous rash, which had extended from it nearly to the umbilicus and half-way down the thigh. Excepting the burning and itching sensation, there was no systemic involvement whatever. On the third day after operation the eruption presented every feature of a severe eczema madidans. Under treatment, in a week resolution had nearly taken place, there still being, however, slight infiltration and scaling. The singular point in this case is that the chaneroids which caused the bubo were promptly healed by iodoform without any unpleasant complication.

CASE XII occurred in the person of a physician, aged thirty-six, who came to me in his fourth year of syphilis. He gives his experience as follows: "Iodoform is to me poisonous in a very high degree. The effects are the same whether I use it locally or whether I only handle it in treating patients. My sufferings are in proportion to the amount of the drug used. About three hours after having used it, a sensation of intense heat is felt in my head. My face becomes flushed, hot, and itchy, my nose and eyes run profusely, and my feet are hot and sore. In the mean time different parts of my body are similarly affected, such as the hands, neck, shoulders, penis, scrotum, and a spot over the sacrum. When this period of heat is in progress, the affected parts become of a deep-red color and excessively itchy. In less than two hours the parts become greatly swollen and covered with myriads of small vesicles, superficial and deep, which contain a yellowish serum. The more superficial vesicles will break of themselves and ooze profusely, an odor of iodine being perceptible. The larger and deeper vesicles, which are seat-

ed on parts with quite thick epidermis, usually fuse together into patches. The process is especially severe upon the fingers and toes and around the matrix of the nails. The nostrils and the inside of the nose for some depth are usually affected very severely, become swollen, oozing, and covered with crusts. This same eczematous condition also affects my face and beard. After several days have elapsed under treatment, the intensity of the morbid process diminishes, the itching and discomfort become less, the swelling slowly subsides, the crusts fall, and in a short time the thickening and redness of the skin disappear. If, however, proper treatment is not adopted, a well-marked eczema results which is exceedingly difficult to cure." On one occasion these toxic phenomena were caused by the patient simply handling a box which contained iodoform, not a particle of which came in contact with his skin. Headache, great weakness, want of appetite, and restlessness are also experienced. This patient thinks that he is more susceptible to the influence of iodoform when he is taking iodide of potassium or some preparation of iodine. I watched the progress of eczema from iodoform in this case, seated on the hand, fingers, and face. It was typical in all its features, and differed from the eruptions of other cases of iodoform poisoning in showing the tendency to chronicity.

CASE XIII occurred in the service of my colleague, Dr. A. W. Stein, in Charity Hospital. It was that of a man, aged thirty, having several chancroids and severe balanitis. A few hours after dressing the parts with a small quantity of iodoform the patient experienced great heat and burning in the penis and scrotum, and an erythema appeared, which promptly developed into typical eczema madidans, which extended nearly to the umbilicus and down the thighs for a few inches. There were no constitutional symptoms. A cure of the rash was effected in about a week.

CASE XIV occurred in the practice of Dr. J. H. Putnam, of Rutland, Vermont. I quote his words: "The patient, a healthy young woman, had catarrh of the middle ear, and I used iodoform dissolved in alcohol upon cotton in an inflator. In about four hours the face began to tingle and burn, and soon became very

painful. This was followed by redness, swelling, and vesiculation, which went on rapidly to pustulation. All these morbid symptoms subsided as rapidly as they appeared. After three weeks a similar application was made to the ear, with the same result as before. A new inflator was used and no bad result followed until it was carelessly put in the same drawer with the old one. Its use was then followed by similar but milder symptoms. During the first attack she had slight febrile action, but there was none afterward."

CASE XV is of especial interest. The patient is a man, sixty-one years of age, who has worked in many minor capacities in Charity Hospital. Seven years ago, when, as boatman, his duties caused him to undergo cold exposure and contact with salt water, he suffered from an ulcer of the leg, which was dressed by one of the orderlies with iodoform ointment. Soon after an acute and severe eczema appeared on the hands and face. This was seen by several of the hospital surgeons, who attributed it to exposure. As the eruption resisted treatment while the man was careful to have his leg dressed with the iodoform salve, and as it grew better and even disappeared when he was irregular or ceased to have the applications made, he became convinced that the iodoform ointment applied to his leg caused the eczema of the hands and face. He discontinued the use of the ointment, and his eczema disappeared without any treatment, after having resisted the most careful use of proper remedies. Four years later he allowed an interne to experiment on him by applying an iodoform ointment to a cut, and as a result was promptly attacked on the face and hands with eczema. In January of this year he received a severe cut on the right wrist, which was dressed by an orderly with iodoform. Within twenty-four hours eczema appeared as before, and ceased on the discontinuance of the use of the drug. There were no systemic symptoms.

A case similar to this is reported by Neisser* as occurring in the person of a colleague who for some months

* "Ueber Iodoform-Exantheme," "Deutsche med. Wochenschrift," July 24, 1884.

suffered from an extensive eczematous eruption, the cause of which and of its continual recurrence they were unable to discover. Later on, when Neisser treated an injury to his patient's foot, he found that he had the iodoform idiosyncrasy, and that his eczema was wholly due to the action of that drug. He has since avoided it, and no longer has the eruption.

CASE XVI.—Fabre* reports the following: A syphilitic man, aged twenty-seven, having suffered from manifestations of an ulcerative and gummatous nature, and also from eczema, had upon the upper lip, near the left commissure, a rupial-looking patch, which was uninfluenced by internal treatment. An ointment of iodoform and benzoated lard (1 to 15) was then applied. Following the first application, an abundant serous discharge was observed upon the sore, and soon the integument of the whole face and head became red and swollen and the seat of exudation and itching. Under appropriate treatment the acute symptoms were relieved in a few days, and the iodoform ointment was again used, when the eczematous eruption appeared again with greater violence. Yet a third time was the same ointment applied with similar results. A strange feature of this case was that a year previously iodoform in powder had been used upon some ulcers without any bad results.

CASE XVII was reported by Fifield.† It was that of a young woman who suffered from deep ecthymatous ulcerations which had resisted mercurials and the iodides. One day several crusts were removed from the hands and from the left temple, and the surfaces left were dusted with iodoform. The next day, as nothing unpleasant had happened, the crusts of three other ulcerations of the scalp were removed and the surfaces were lightly dusted with the powder. Within a few hours the whole scalp became swollen and exuded a profuse serous discharge,

* "Éruption eczémateuse provoquée par l'application d'une pommade à l'iodoforme chez un syphilitique," *"Gazette méd. de Paris,"* October 11, 1884.

† "Boston Med. and Surg. Journal," March 16, 1882.

and, in fact, presented the appearance of an acute eczema. There were no constitutional manifestations. The eruption disappeared in a week.

CASE XVIII, reported by Goodell,* was that of a woman, forty years old, of irregular habits, who had had, seven years previously, ragged and indolent ulcers, which had left scars. In August, 1881, she had a ragged ulcer of more than an inch in diameter on the chin, a little to the left of the median line. Various modes of treatment having failed, in the following March an ointment—an iodoform ointment (fifteen grains to the ounce)—was ordered. After its use for nine days the face became red, swollen, and covered with vesicles, and from it exuded a yellow serum. The eruption was accompanied by intense smarting and burning and a sense of tightness of the skin. The patient became slightly delirious, with weak and irregular pulse.

CASE XIX is Janowsky's sixth case. A girl, sixteen years old, anæmic and neurotic, had a patch of lupus tubercles and ulcers on the right thigh, which were scraped, scarified, and dressed with iodoform. Three days later purpuric spots appeared over the surrounding skin, and continued to develop as far up as the breasts. Discontinuance of the use of the drug was followed by the disappearance of the spots. Fourteen days later it was applied again, with the same result as at first. There was no elevation of temperature, nor rheumatism, nor were there any symptoms pointing to purpura rheumatica.

CASE XX is one of the four cases reported by Hoepfl † of systemic iodoform poisoning. The patient was a woman, aged thirty-seven, whose breast was amputated and the wound dressed with iodoform (ten grammes) and iodoform gauze. Severe sensory disturbances were developed, and an exanthem of red spots over the whole body appeared. Death took place on the thirteenth day. Fatty degeneration of the heart, liver, and kidneys was found.

A clear idea of the most important features of these cases is given in the following table.

* "Boston Med. and Surg. Journal," April 9, 1885.

† "Aerztl. Intelligenz-Blatt," xxx, München, 1883.

No.	Reported by—	Sex.	Age.	Nature of skin lesion.	Time of appearance.	Constitutional symptoms.
1	Taylor.	M.	21	Intense erythema.	3 hours.	None.
2	"	M.	32	Erythema scarlatini-forme.	Few hours.	Anorexia, fever, headache, and giddiness
3	"	F.	28	Erythema erysipelatos.	2 days.	Vomiting, diarrhœa, headache, delusions, fever.
4	"	F.	26	Erythema multiforme.	12 days.	Fever, malaria, dizziness, and drowsiness
5	"	M.	34	Erythema scarlatini-forme.	Second day.	None.
6	Zeissl.	M.	3	Erythema.	14 days.	High fever, vomiting, & albuminous urine
7	"	M.	36	Erythema urticatum.	10 days.	
8	Janowsky.	M.	28	Erythema.	Probably 1 day.	Fever.
9	"	M.	22	Papular erythema.	24 hours.	None.
10	"	M.	31	Erythema.	48 hours.	None.
11	"	M.	24	Papular erythema.	Third day.	Fever.
12	"	M.	48	Erythema bullosum.	Third day.	Mild fever.
13	Köster-Syke.	M.	Not given.	Erythema bullosum.	Short time.	Not given.
14	Treves.	F.	13	Papular and vesicular erythema.	14 days.	Fever, headache, and giddiness.
15	Taylor.	M.	27	Eczema madidans.	1 day.	None.
16	"	M.	36	Eczema madidans.	3 hours.	Headache, loss of appetite, nervousness, and malaria.
17	Taylor & Stein.	M.	30	Eczema madidans.	Few hours.	None.
18	Putnam Hitherto unpub.	F.	About 20	Eczema rubrum.	Few hours.	Slight fever.
19	Taylor.	M.	61	Eczema madidans.	Few hours.	None.
20	Fabre.	M.	27	Eczema madidans.	24 hours.	
21	Fifield.	F.	Yung	Eczema madidans.	24 hours.	None.
22	Goodell.	F.	40	Eczema madidans.	9 days.	Mild delirium, weak and irregular pulse.
23	Janowsky.	F.	16	Purpuric spots.	Third day.	None.
24	Hoepl.	F.	37	Red spots.	Uncertain.	Death on 10th day; fatty degeneration of heart, liver, and kidneys.

In sixteen of these cases we find the association of constitutional symptoms in varying degrees with a well-marked exanthem. In nine cases the rash existed alone, without any apparent systemic reaction to the toxic agent. As a corollary to this we have the facts presented by the statistics compiled by Cutler* in his admirable article on "Iodo-

* "Boston Medical and Surgical Journal," July 29 and August 5, 1886.

form Poisoning," which should be widely read, in which are given the main points of seventy-seven cases, all of them showing more or less grave constitutional disturbance, and yet in but five of them was there a history of a co-existent rash. The same features are presented by the more recent statistics of Willemer.* The conclusion is obvious that the toxic effects of iodoform are observed more frequently in the form of systemic involvement than in that of cutaneous manifestations, and, further, it may be said that it may set up inflammatory disturbances of the skin without any apparent constitutional reaction.

The nature of the skin lesions due to this agent may be concisely stated under the head of dermatitis; but they may, for the sake of accuracy, be further subdivided as follows, according to their relative frequency: First, erythema; second, eczema; and third, purpuric spots.

The erythemata due to iodoform present many of the features of similar simple eruptions, and to those due to other drugs. Their mode of invasion is prompt, and their extension rapid. They may increase from an original focus of contact with the drug, and extend over parts of or over the whole body, or they may also thus begin and be met with patches which have developed in parts remote from the point of invasion. Then, again, a more or less general erythematous rash may follow the simple act of smelling the agent, without any contact whatever. Reaching their full evolution in one or several days, they, under favorable circumstances, rapidly undergo involution, behaving much like the ordinary erythemata, except that their course is usually even more rapid.

Various forms of erythema have been noted. In some instances it is a very superficial and comparatively mild, pinkish exanthem; in others it is still superficial in charac

* "Centralblatt für Chirurgie," No. 50, 1886.

ter, but very deep in hue, and may be termed scarlatini-form, so great is the dermal congestion. Then, in rather exceptional cases, and usually in those presenting more or less grave constitutional symptoms, the erythema presents, in its hue and brawny feel, points of resemblance to erysipelas. While some cases have presented lesions similar to erythema iris and erythema urticatum, others have been observed of the papular, vesicular, and bullous forms, and come under the head of erythema multiforme. The toxic action of iodoform, therefore, may show itself on the skin in all of the forms of erythema.

The eczema caused by iodoform is usually of severe form and of rapid evolution. It may begin at the point of contact with the drug, or it may develop in parts far distant, or again appear in one or in several spots—such as the hands, face, and trunk—simply from smelling of the drug. Its character is pronounced from the first; much surface is rapidly involved; the erythema and infiltration go promptly on to vesiculation and the formation of a well-marked weeping surface, in all respects similar to the ordinary eczema madidans. In most cases the involution is almost as rapid as the evolution, provided the toxic agent is removed. But in some instances, perhaps of debility of marked eczematous tendency, or of excessive idiosyncrasy, the affection shows a tendency to become chronic. It is usually very amenable to treatment. My statistics show that eczema occurred nine times in twenty-four cases, being a ratio of forty-three in a hundred.

I am unable from my own observation to say anything as to the occurrence of purpuric spots as a result of iodoform intoxication. Janowsky reports such a case, in which the spots appeared on the third day, strange to say, without any co-existent systemic symptoms. Further observation is necessary upon this branch of the subject.

A mild form of erythema is often seen on the hands of dressers, nurses, and orderlies in hospitals, and of those who manufacture iodoform gauze, which has no specific characteristics whatever, and is comparable to the simple irritation produced by any drugs, such as mustard or the tarry preparations.

The date of appearance of these iodoform exanthems is interesting. In twelve cases the rash began within a few hours on the first day, in three on the second, three on the third, one on the ninth, one on the tenth, one on the twelfth, and in two on the fourteenth day. In one half of them, therefore, we find that the toxic action began very early. This is in marked contrast with the statistics of the cases of systemic poisoning, in the majority of which the morbid symptoms began in the second week. As a rule, it may be stated that, in proportion as the rash is slow in appearing, so are the concomitant symptoms severe. The cases reported seem to warrant the belief that the earlier the date of evolution of the rash, the more general and exanthematic it is.

The age of those patients showing a tendency to this form of toxic action of iodoform is noteworthy. Three patients had not yet reached puberty, eleven were between twenty and thirty, seven were between thirty and forty, and one was sixty-one years of age. The statistics seem to show that this form of intoxication is most frequent in youth and middle age, in contrast with the severe forms, which occur more often in the aged.

The concomitant symptoms present much variation, since in nine cases they were absent, were mild in eight, and severe in five cases, in one of which death occurred.

It is probable that we shall have no more of those dreadful fatal cases, since we have now learned how to use the agent intelligently, and since it has been largely re-

placed by the bichloride dressing. Though thus limited, its use will still be very extended, since its action in promoting healthy granulation is more efficient than that of any other known agent. While we certainly shall not use quantities such as one hundred to two hundred grammes, which, strange to say, in some cases have produced no untoward results, we must bear in mind the fact that grave symptoms of poisoning have followed the use of fifteen grains and less.

The systemic symptoms presented in the foregoing cases varied considerably in degree. I am in accord with Cutler, who adopts Nussbaum's division of the symptoms of iodoform poisoning, making three degrees.

The first is comparatively mild. A loss of appetite, headache, disturbance of disposition by excitation or depression, a mild delirium or loss of memory, and sleeplessness may be observed.

In the second degree there are absolute anorexia, an intensification of the head symptoms, perhaps dementia, mania, or melancholy, weak and rapid pulse, mild fever, and emaciation.

The third degree is a continuation and intensification of the second. Such patients lie perfectly abject in sopor, with a rapid, thready pulse and a cold surface, and die in collapse.

The systemic symptoms in the majority of cases of iodoform exanthems belong to the first and second degree. In but one case did they go on to the third degree and end in death.

The origin of these exanthems in the toxic action of iodoform being beyond dispute, the interesting question suggests itself, In what way does the drug act? Certain of the cases show that at a given spot irritation of a high grade began, and from that form extended until much sur-

face was involved in acute inflammation. The morbid process is, therefore, what is termed "contagion by continuity," in which healthy areas around a morbid one become affected. It is simply a local inflammatory process. This form of iodoform rash, itself an eczema, has its analogue in the eczema caused by mercurial ointment.

The diffused erythematous rashes of iodoform and the eczematous form developing at several different sites can hardly be accounted for in this manner. Their history shows, as a rule, that there is more or less systemic reaction, and that they are probably angeio-neuritic in origin. They have their analogues in the quinine and antipyrine exanthems. The same origin undoubtedly exists in the cases in which the mere smelling of the drug gives rise to severe local and general symptoms. Iodoform exanthems have no points of resemblance to those of iodide of potassium except in the erythema, but differ in being more ephemeral and less prone to hæmorrhagic exudation.

A consideration of all the facts presented by the foregoing cases shows clearly that, if we attempt to explain the ultimate origin of the morbid phenomena by the term idiosyncrasy, we must concede much latitude to that vague factor. In most of the cases of eczema caused by iodoform I am of the opinion that the irritating influence of the drug is equally an important factor as the individual peculiarity, and that the same facts apply to eczema provoked by mercurial ointment.

The cases, however, which, for want of a more precise term, I designate as of angeio-neuritic origin, can only be explained by the term idiosyncrasy or the mystery of individuality. I think that too much stress has been laid upon this indefinite factor by writers upon the severer forms of iodoform poisoning. In most of the cases the agent acted as a poison pure and simple. In those instances in

which large quantities of the drug were used with impunity the probability is that for some occult reason absorption did not take place. Certain it is that, in all experiments on animals, where the agent was administered by the mouth or by subcutaneous injection, toxic phenomena promptly followed.

The practical lessons taught by the collective knowledge of the nature and action of iodoform should be well remembered, and may be concisely stated as follows :

A. Its use is indicated : 1. On fresh wounds.

2. On diseased surfaces—gangrenous, chancroidal, phagedenic, syphilitic, tuberculous—and on those slow to take on healthy granulation.

3. On the surface of necrosed bone.

B. Its use is contra-indicated : 1. On freshly cut bone.

2. On granulating surfaces.

3. In cases in which it is known or is found to produce toxic effects.

C. Modes of use : 1. It should be dusted on the surface lightly and sparingly.

2. In wound-cavities or in the natural cavities as small a quantity as possible should be employed ; in the former it is preferable to use it in the form of gauze.

3. It should never be rubbed in with the finger.

4. Its application should be renewed as infrequently as possible.

5. Such aids to absorption as tightly fitting bandages and impermeable dressings should not be used.

6. Its use should be discontinued as soon as healthy granulations appear.

7. It should not be used coincidently with any other antiseptics, carbolic acid especially (Mösetig-Moorhof).

8. It should be used with great caution in the young and the old, in anæmic and neurotic persons, and those suf-

fering from weak heart or Bright's disease; also in very fat and flabby subjects.

9. Should toxic symptoms appear, the iodoform dressing must be promptly and thoroughly removed.

D. The occurrence of anomalous forms of persistent or recurrent eczema in persons who handle or in any way come in contact with the drug, or who use it as an ointment or in suppositories in the vagina or rectum, should cause the physician to suspect the agent as the possible cause.

E. It is most important that the practitioner should exercise a watchful care over all patients for whom he prescribes this agent, and should he observe morbid symptoms, however mild, pointing to the brain, heart, or lungs, or a tendency to loss of appetite or emaciation, he should cause the discontinuance of its use at once.

F. The treatment of the skin manifestations is similar in all respects to that of the simple eruptions of the same varieties. Systemic poisoning should be treated symptomatically, since we have no specific.

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